

Amendments to the Claims:

Please amend Claims 5-18. Please add new Claims 22-28. The Claim Listing below will replace all prior versions of the claims in the application:

Claim Listing:

Claim 1 (original): A method of stimulating cartilage growth or repair at a site in a subject in need of such growth or repair, said method comprising the step of administering to the site a therapeutically effective amount of an agonist of the non-proteolytically activated thrombin receptor.

Claim 2 (original): The method of Claim 1 wherein the site is an arthritic joint.

Claim 3 (original): The method of Claim 1 wherein the site is being treated for cartilage damage or loss.

Claim 4 (original): The method of Claim 1 wherein the site is being treated for cartilage damage or loss due to traumatic injury.

Claim 5 (currently amended): The method of Claim 1 wherein the agonist is a thrombin peptide derivative, or a physiologically functional equivalent thereof, comprising a polypeptide represented by the following structural formula:



wherein R is a serine esterase conserved sequence.

Claim 6 (currently amended): The method of Claim 5 wherein the agonist consists of ~~thrombin peptide derivative~~ has between about 12 and about 23 amino acids.

Claim 7 (currently amended): The method of Claim 6 wherein the serine esterase conserved sequence consists of ~~has~~ the amino acid sequence of ~~SEQ ID NO. 1~~

SEQ ID NO.:1 (Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val), or a C-terminal truncated fragment thereof consisting of having at least six amino acids, provided that zero, one, two or three amino acids in the serine esterase conserved sequence differ from the corresponding position of ~~SEQ ID NO.:1~~ SEQ ID NO.:1.

Claim 8 (currently amended): The method of Claim 6 wherein the serine esterase conserved sequence consists of has the amino acid sequence of ~~SEQ ID NO.:1~~ SEQ ID NO.:1 (Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val), or a C-terminal truncated fragment thereof consisting of having at least nine amino acids, provided that zero, one or two of the amino acids in the serine esterase conserved region are conservative substitutions of the corresponding amino acid in ~~SEQ ID NO.:1~~ SEQ ID NO.:1.

Claim 9 (currently amended): The method of Claim 6 wherein the serine esterase conserved sequence consists of has the amino acid sequence of ~~SEQ ID NO.:2~~ SEQ ID NO.:2 (Cys-X₁-Gly-Asp-Ser-Gly-Gly-Pro-X₂-Val, wherein X₁ is Glu or Gln and X₂ is Phe, Met, Leu, His or Val), or a C-terminus truncated fragment of ~~SEQ ID NO.:2~~ SEQ ID NO.:2, said fragment consisting of having at least six amino acids.

Claim 10 (currently amended): The method of Claim 9 wherein the agonist thrombin peptide derivative comprises the amino acid sequence Arg-Gly-Asp-Ala (~~SEQ ID NO.:3~~) (SEQ ID NO.:3).

Claim 11 (currently amended): The method of Claim 10 wherein the agonist thrombin peptide derivative comprises the amino acid sequence Arg-Gly-Asp-Ala-Cys-X₁-Gly-Asp-Ser-Gly-Gly-Pro-X₂-Val (~~SEQ ID NO.:4~~) (SEQ ID NO.:4), wherein X₁ is Glu or Gln and X₂ is Phe, Met, Leu, His or Val.

- Claim 12 (currently amended): The method of Claim 11 wherein the agonist consists of ~~thrombin peptide derivative~~ has the amino acid sequence Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-~~(SEQ ID NO 5)~~ (SEQ ID NO.:5), or an *N*-terminal truncated fragment thereof, provided that zero, one, two or three amino acids at positions 1-9 in the agonist ~~thrombin peptide derivative~~ differ from the amino acid at the corresponding position of ~~SEQ ID NO 5~~ SEQ ID NO.:5.
- Claim 13 (currently amended): The method of Claim 11 wherein the agonist consists of ~~thrombin peptide derivative~~ has the amino acid sequence Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-~~(SEQ ID NO 5)~~ (SEQ ID NO.:5), or an *N*-terminal truncated fragment thereof, provided that zero, one or two amino acids at positions 1-9 in the agonist ~~thrombin peptide derivative~~ are conservative substitutions of the amino acid at the corresponding position of ~~SEQ ID NO 5~~ SEQ ID NO.:5.
- Claim 14 (currently amended): The method of Claim 12 wherein the agonist ~~thrombin peptide derivative~~ is administered in a pharmaceutical composition additionally comprising an implantable, biocompatible carrier.
- Claim 15 (currently amended): The method of Claim 14 wherein the carrier comprises a ~~polylactic acid/polyglycolic acid homopolymer~~ polylactic acid homopolymer, polyglycolic homopolymer or copolymer .
- Claim 16 (currently amended): A method of stimulating cartilage growth or repair at a site in a subject ~~in need there such growth or repair~~ in need of such growth or repair, said method comprising the step of administering to the site a therapeutically effective amount of an agonist of the non-proteolytically activated thrombin receptor, wherein said agonist consists of a peptide having the sequence Ala-Gly-

Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val (~~SEQ ID NO 5~~) (SEQ ID NO.:5).

Claim 17 (currently amended): A method of stimulating cartilage growth at an arthritic joint in a subject, said method comprising the step of administering to the site a therapeutically effective amount of an agonist of the non-proteolytically activated thrombin receptor, wherein said agonist consists of a peptide having the sequence Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val (~~SEQ ID NO 5~~) (SEQ ID NO.:5).

Claim 18 (currently amended): A method of stimulating cartilage growth in a subject at a site being treated for cartilage loss, said method comprising the step of administering to the site a therapeutically effective amount of an agonist of the non-proteolytically activated thrombin receptor, wherein said agonist consists of a peptide having the sequence Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val (~~SEQ ID NO 5~~) (SEQ ID NO.:5).

Claim 19 (currently amended): A method of stimulating cartilage growth in a subject at a site being treated for cartilage loss due to traumatic injury, said method comprising the step of administering to the site a therapeutically effective amount of an agonist of the non-proteolytically activated thrombin receptor, wherein said agonist consists of a peptide having the sequence Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val (~~SEQ ID NO 5~~) (SEQ ID NO.:5).

Claim 20 (original): A method for culturing chondrocytes *in vitro*, the improvement comprising culturing the chondrocytes in the presence of a stimulating amount of an NPAR agonist.

- Claim 21 (original): The method of Claim 20, further comprising the step of administering a therapeutically effective amount of the cultured chondrocytes to a site in a subject in need of cartilage repair or growth.
- Claim 22 (new): The method of Claim 6, wherein the subject is administered a therapeutically effective amount of a physiologically equivalent agonist comprising a C-terminal amide.
- Claim 23 (new): The method of Claim 6, wherein the subject is administered a physiologically functional equivalent agonist comprising Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-CONH₂ (SEQ ID NO.:6).
- Claim 24 (new): The method of Claim 6, wherein the subject is administered a physiologically functional equivalent agonist consisting of Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-CONH₂ (SEQ ID NO.:6).
- Claim 25 (new): A method of stimulating cartilage growth or repair at a site in a subject in need of such growth or repair, said method comprising the step of administering to the site an agonist of the non-proteolytically activated thrombin receptor, wherein said agonist consists of the sequence Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-CONH₂ (SEQ ID NO.:6).
- Claim 26 (new): A method of stimulating cartilage growth at an arthritic joint in a subject, said method comprising the step of administering to the site a therapeutically effective amount of an agonist of the non-proteolytically activated thrombin receptor, wherein said agonist consists of the sequence Ala-Gly-Tyr-Lys-Pro-Asp-

Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-CONH₂ (SEQ ID NO.:6).

Claim 27 (new): A method of stimulating cartilage growth in a subject at a site being treated for cartilage loss, said method comprising the step of administering to the site a therapeutically effective amount of an agonist of the non-proteolytically activated thrombin receptor, wherein said agonist consists of the sequence Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-CONH₂ (SEQ ID NO.:6).

Claim 28 (new): A method of stimulating cartilage growth in a subject at a site being treated for cartilage loss due to traumatic injury, said method comprising the step of administering to the site a therapeutically effective amount of an agonist of the non-proteolytically activated thrombin receptor, wherein said agonist consists of the sequence Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-CONH₂ (SEQ ID NO.:6).